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Focal knee resurfacing and effects of surgical precision on opposing cartilage. A pilot study on 12 sheep

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Background: Full thickness cartilage lesions (ICRS grade 3–4) and focal lesions of degenerative origin may progress to osteoarthritis (OA). Such focal lesions can be treated by metallic implants. We hypothesized that such treatment results in opposing surface cartilage damage that correlates with implant position (height) relative to the adjacent cartilage surface. This relationship was investigated using a sheep animal model.

Methods: Both medial femoral condyles of 12 sheep were operated. The implants, were inserted in the weight-bearing surface at different heights relative to the surrounding cartilage. Euthanasia was performed at 6 or 12 weeks. After retrieval, implant height was analyzed using laser scanning. Damage to the opposing tibial cartilage was evaluated macroscopically and microscopically according to the modified Mankin score.

Results: Twenty-two knees were available for evaluation and showed cartilage lesions ranging from severe damage (Mankin stage 11) to almost pristine conditions (Mankin stage 1). There was a strong correlation between implant height and cartilage damage. Standard deviation from the aimed implant height was 0.47 mm.

Conclusions: Our results showed significant surgical imprecision and protruding implants imposed severe cartilage damage. We therefore suggest implants should be placed recessed (approx. 0.5 mm) below the surrounding cartilage in this animal model. These results encourage further studies of metallic implants yet the utmost precision regarding position is required.

Introduction

Articular cartilage is a remarkable tissue capable of enduring great loads over numerous and varying cycles during a lifetime. However, cartilage has a poor healing capacity even after minor injuries, and more severe lesions, i.e., large full thickness defects, left untreated do not heal but may progress to osteoarthritis (OA)[1–7]. Also, even with various kinds of treatments, it has been suggested that such lesions progress to OA[8–10]. Focal cartilage injuries in the knee are common joint disorders causing pain and disability and are associated with a major disease burden including socio-economic impact[11–13] (www.arthritis.org; March 2005). In patients with advanced disease knee arthroplasty has a radical effect, but is seldom indicated at an earlier stage where a less invasive or intermediate treatment is needed. Hence early treatment can be suggested both for prophylactic and symptomatic reasons[14].

Primary surgical treatment methods typically aim at biological repair and include debridement and subchondral drilling (microfracture)[15] or cartilage reconstructive methods such as osteochondral autografts (mosaicplasty)[16] or chondrocyte transplantation[17]. Clinically, these biological methods can provide significant improvement for the patient but results seem to be less satisfying with increasing patient age[9,15,18,19]. These methods demand meticulous rehabilitation programmes, are technically demanding or use sophisticated laboratory resources. According to a recent Cochrane review there is insufficient evidence to conclude which treatment method for full thickness articular cartilage lesion in the knee is superior[20].

An alternative strategy for the symptomatic middle-aged patient or when previous methods have failed is using focal knee

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resurfacing (FKR) implants that can be inserted by a single surgical procedure providing immediate stability. We have probed the possibility of resurfacing focal cartilage lesions with a metal implant, inserted into a surgically created defect using a sheep model. To our best knowledge there are currently three groups in the world aiming at resurfacing focal knee lesions[21–23]. The concept of an implant articulating against the opposite cartilage (unipolar) constitutes three fundamental issues, the successful solution of which is an unconditional prerequisite. First, the implant must bond to the host bone in a satisfactory way. Second, the adjacent cartilage must interface with the biomaterial and, third, the opposing cartilage must withstand the implant biomaterial.

This pilot study on sheep concerns the last issue; we investigated the effect of FKR implants on the opposing cartilage and related these effects to the implant height. It was believed that a unipolar implant should not protrude above the surrounding cartilage surface, as it would be liable to damage the opposing tibial cartilage. Most authors have acknowledged this fact, and aim at inserting the implant either flush or somewhat below the surrounding surface[21,22,24]. We hypothesize that there is a correlation between implant position and cartilage wear.

Materials and methods

Animals

Twelve healthy female sheep (Swedish landrace) from the same breeder were used in the study. The mean age and weight of the sheep were 5 years (range 5–7) and 82.5 kg (range 70–99), respectively. The animals were housed at the Department of Clinical Sciences, Swedish University of Agriculture Sciences (SLU) in Uppsala, Sweden. They were kept indoors in stables in groups of three. Food was given twice a day and water was freely available to the sheep. They were well acquainted with the person handling them. They were observed daily to monitor the animals' general condition, signs of pain and lameness. Animal Ethics Committee, Uppsala Sweden, approved the protocol.

Implant

The monobloc implants were manufactured and provided by Episurf AB, Stockholm, Sweden. Two types of implants were used (Fig. 1). The first batch (outer diameter 10 mm, hemispherical radius of 17 mm) was manufactured using Spark Plasma Sintering (SPS) technique with a gradient powder blend of 50% hydroxyapatite (HA) at the non-articulating surface and pure stainless steel (316L) towards the joint cavity. The articulating surface was polished to a roughness (R_a) <0.03. These were implanted in the first six animals. The second batch (diameter 7.5 mm) had a double-curved (radii 19 and 12 mm) computer-aided design/computer-aided manufacturing (CAD/CAM) modelled articulating surface, according to computed tomography (CT) scans of a standard sheep knee and manufactured from implant-grade Cr–Co with a coating of plasma sprayed HA (Plasma Biotal Ltd. Buxton, GBR). These were implanted in the last six animals. For primary fixation the implants have an HA coated peg (10 mm in length and 2 mm in diameter) that was press-fitted into an undersized (diameter 1.8 mm) drill hole in the bone.

Anaesthesia

Anaesthesia was induced with an intravenous injection in the jugular vein of xylazin (Rompun® vet, Bayer Animal Health, Lyngby, Denmark) 0.11 mg/kg and ketamine (Ketaminol® vet, Intervet, Stockholm, Sweden) 2.2 mg/kg. After intubation the anaesthesia was maintained with isoflurane (IsoFlo® vet, Orion Pharma Animal Health, Stockholm, Sweden) in 1.5–3% in 100% oxygen. All sheep breathed spontaneously. When the animals were anesthetized blood samples were taken from the cephalic vein. They were given one dose antibiotics preoperatively, cefuroxim (Cefuroxim, Farmaplus, Oslo, Norway) 22 mg/kg IV and analgesic, carprofen (Rimadyl® vet, Orion Pharma Animal Health, Stockholm, Sweden) 4 mg/kg SC, buprenorfin (Temgesic®, Schering-Plough, Stockholm, Sweden) 0.01 mg/kg IM, glykopyrron (Robinul®, Meda, Solna, Sweden) 0.25 ml/10 kg SC. The surgical field was aseptically prepared and they were placed in the operating room in dorsal recumbence.

Surgery

Surgery was performed on both knees, starting with the right or left knee arbitrarily. All operations were carried out by the same surgeons (HNS, NMC and LR) and performed under aseptic conditions. The medial femoral condyle was exposed through a medial parapatellar 5–6 cm incision through skin and subcutaneous tissue.

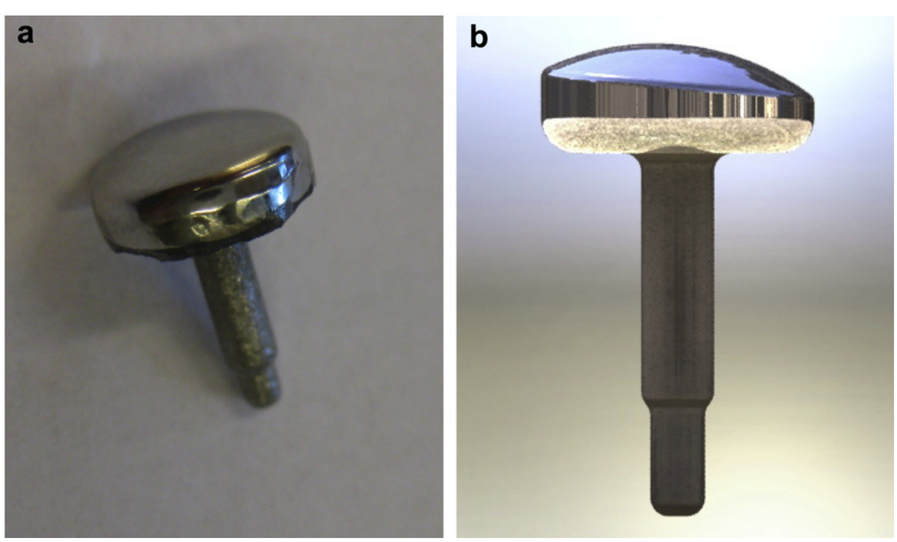

Fig. 1. (a) Shows the first generation hemispherical steel-HA gradient implant. (b) Shows the second generation HA coated Cr–Co implant, characterized by the double-contoured articulating surface. Both implants use a press-fit peg for primary fixation.

After inspecting the knee a centralizing device, adapted to the contour of the posterior weight-bearing condylar surface was applied and a 1.8 mm hole was drilled approximately 10 mm deep in which a steering pin was inserted. A sharp cylinder was passed onto the pin in order to sharply cut the edges of the cartilage in a diameter coinciding with the size of the implants. We hypothesized an ideal implant level of 0.5 mm recessed; arbitrarily chosen to represent approximately 50% of the actual condyle cartilage thickness. Thus a defect was created using an in-house specially designed reamer in order to obtain different depths aiming to place the implants flush, 0.3 or 0.7 mm below the surrounding cartilage surface, respectively. Those recessed levels were chosen on equal distance from the 0.5 mm ideal level; the actual levels were to be determined by laser measurements. A dummy was then used to control the position before final insertion of the implant with press-fit technique. The joint capsule was sutured in a continuous pattern using polydioxanone (PDS®, Ethicon) and the subcutaneous tissue and skin was closed in a similar pattern using polyglecaprone 25 (Monocryl®, Ethicon). No surgical complications occurred during the operations. The sheep were extubated in their stables and under continuous observation resumed consciousness within 1 h post surgery. The animals were sacrificed at 6 weeks (three animals batch 1 and six animals batch 2) or 12 weeks (three animals batch 1) weeks using an overdose pentobarbital (100 mg/ml) after securing blood samples. The knees were removed from the body and macroscopic and histological assessments were performed.

Laser measurements of implant position

The medial femoral condyle of both knees was used for analysis. A negative print was taken of the medial femoral condyle using an alginate plaster (Hydrogym; Zhermack, Badia Polesine, Italy), which was then scanned using a high precision (<1 μm) laser scanner device (www.nikonmetrology.com; LK, Scandinavia, Stockholm, Sweden). The contour of the femoral condyle including the implant was digitized using a specific software program (Metris Focus Inspection 9.2) and the radius of the condyle curvature was determined in both the sagittal and coronal planes. The surface of the implant was then marked with five different reference points in the implant (mid-point of implant and anterior, posterior, medial and lateral edge). From these landmarks the implant height (μm) relative to the surrounding cartilage surface was calculated (Fig. 2). For technical reasons two implants could not be analyzed.

Macroscopic cartilage evaluation

High-resolution photographs (Canon EOS 450D, EF-S 17–55 mm f/2.8 IS USM lens fixated at a distance of 0.3 m, using 35 mm focal length) were taken of the medial (Fig. 3) and lateral femoral and tibial condyles. Two blinded independent observers (NMC & HB) evaluated the photographs of each tibia plateau separately. Articular cartilage lesions were classified according to a scale 0–4, grade 0 is normal, grade 1 is softening and fibrillation, grade 2 is superficial fissures (not reaching the subchondral bone), grade 3 fissures to the subchondral bone and grade 4 exposed subchondral bone[25–27].

Microscopic cartilage evaluation

After removal of soft tissues and photography, the articular cartilage of the tibia was dissected and placed in 2% glutaraldehyde + 1% paraformaldehyde in 0.1 M sodium cacodylate buffer, pH 7.4 and stored in refrigerator. Small pieces chosen to represent areas of cartilage facing the implants were cut and rinsed in 0.1 M phosphate buffer, pH 7.4 post-fixed in 2% osmium tetroxide 0.1 M phosphate buffer, pH 7.4 at 4°C for 2 h, dehydrated in ethanol followed by acetone and embedded in LX-112 (Ladd, Burlington, Vermont, USA). Semi-thin sections were cut and stained with toluidine blue and used for light microscopic analysis. Digital images were taken by using a Morada camera (Olympus Soft Imaging Solutions, GmbH, Münster, Germany). Damage to the cartilages were evaluated according to a modified Mankin score (the smear layer and calcified zone is not evaluated; grade 0–12: grade 0 is normal cartilage and grade 12 is totally deranged cartilage)[28,29].

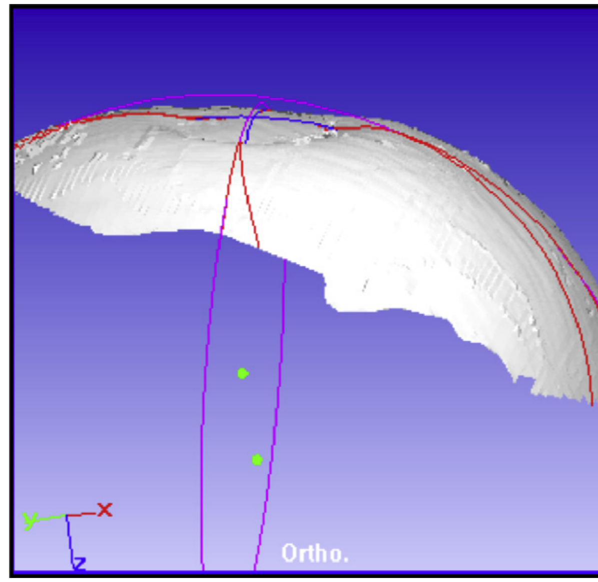

Fig. 2. Postoperative laser measurements to evaluate implant position. The purple circles show the radius of the original cartilage level and the blue lines underneath show the implant level.

Statistical methods

Student's *t* test was used for comparisons between groups. Linear regression was used to assess the relationship between implant position and cartilage damage. Means for each animal were used as independent samples. The calculation was performed using STATA v12.1 with the procedure for linear least square regression. Data were compensated for heteroscedasticity and absence of normal distributed residuals using Huber–White Sandwich Estimator. The estimation uncertainty is presented by its *P*-value and 95% confidence interval.

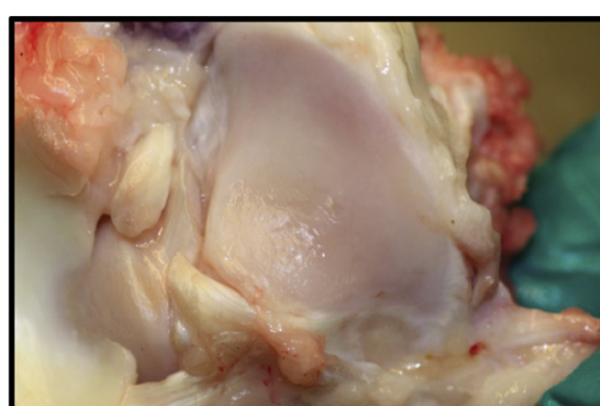

Fig. 3. High-resolution photograph used to evaluate cartilage damage of the opposing tibial condyle. Here, macroscopic cartilage damage grade 1.

Results

One sheep was euthanized immediately after the operation due to an anaesthesiologic complication. All wounds healed without complications and no signs of infection were observed. Thus, 22 knees in 11 animals were available for macroscopic and microscopic evaluation, and because two samples could not be digitized, 20 knees remained for laser measurement. No histological differences in opposing tibial cartilage were seen between the two types of implants used ($P = 0.82$; from 10 samples of comparable implant heights). Mankin score after 12 weeks did not grossly differ from 6 weeks (mean 6.7, 5.5, respectively, $P = 0.61$; batch 1). Therefore data are presented as one pooled group of implants.

Implant position

Height of implants ($n = 20$) as assessed by the mean of the three transversal data points from laser scans averaged standard deviation (SD) −0.20 (0.66) mm in the group aimed at flush position, −0.33 (0.18) in the group aimed for 0.3 mm recessed and −0.76 (0.12) in the group aimed for 0.7 mm recessed, respectively. Implant position expressed with the aimed offset level subtracted, averaged for the merged group, was −0.12 (0.47) mm (Fig. 4). In fact 80% of the implants were placed somewhat lower than aimed for but some implants protruded up to 0.7 mm above the intended position.

Macroscopic cartilage evaluation

Macroscopic score ($n = 11$) averaged (range) 1.7 (1–3). Macroscopic score as a function of implant position showed a linear relationship ($P = 0.01$) such that International Cartilage Research Society (ICRS) score increased by 1.2 (95% conf. int: 0.4, 2.0) units per each mm increase in implant height (Fig. 5).

Microscopic cartilage evaluation

Histological preparation showed a varying degree of surface damage [Fig. 6(a) and (b)]. Modified Mankin score ($n = 11$) averaged (range) 4.8 (1–10), and protruding implants showed higher Mankin score ($P < 0.01$). Microscopic score as a function of implant position showed a linear relationship ($P = 0.008$) such that Mankin score increased by 4.3 (95% conf. int: 1.5, 7.0) units per each mm elevation in implant height (Fig. 7).

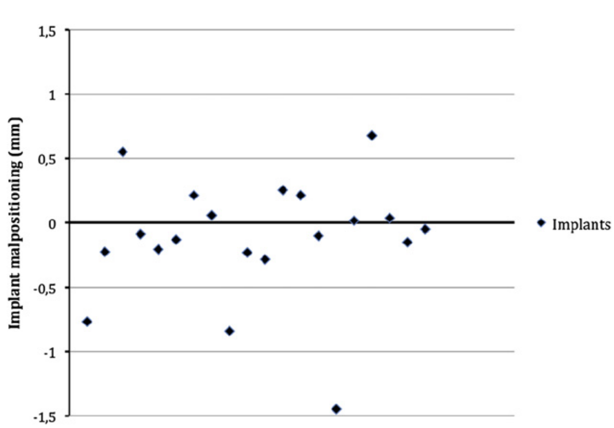

Fig. 4. Implant deviation (*Y*-axis) from intended position for each implant ($n = 20$); height expressed with the aimed offset level subtracted.

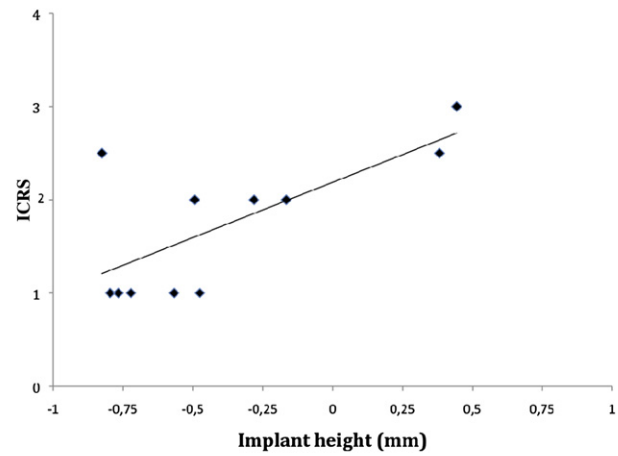

Fig. 5. Macroscopic cartilage damage correlated to implant position. *X*-axis shows implant height in mm. *Y*-axis shows the macroscopic cartilage score (ICRS) where 0 is normal cartilage and 4 is exposed bone. Line denotes best fit for least square regression.

Discussion

In this pilot study we investigated the effect of FKR implants on the opposing cartilage. It was recognized that a unipolar implant should not protrude, as suggested by previous investigators who aimed to insert the implants either flush or recessed[21,22,24]. To our knowledge, however, there are no previous reports where the implant position has actually been accurately measured postoperatively. With such precise measurements, our hypothesis was confirmed: we found a statistically significant correlation between implant position and opposite cartilage wear.

This first report shows that precise implant positioning is hard to achieve consistently and, moreover, damage to the opposing cartilage appears to be distinctly sensitive to implant position. We found that one out of five implants were protruding and that all protruding implants, showed signs of significant cartilage damage on the opposing articulating surface both macroscopically and microscopically. On the other hand 20% of all implants showed an almost pristine (Mankin 1) opposing cartilage provided the implants were moderately recessed.

Previous studies discuss the importance of implant height in relation to surrounding cartilage, where implant insertion was aimed at different levels[21,22,30]. One animal study[22] suggested increased opposing cartilage damage when implants were seated too deep. Our results are compatible with that study. One implant unintentionally seated too deep showed a considerable degree of cartilage wear on the opposing tibial cartilage. We reason that a deeper recessed implant would resemble that of a full thickness chondral defect, where the cartilage edges around the lesion become overburdened and degenerate as previously suggested[22,31]. Further, a randomized study on goat[30] found less cartilage damage in the implant group compared to an untreated defect or to a defect treated with subchondral bone stimulation. Our study did not have the statistical power to prove this point. Hitherto, no data exist regarding optimum implant position.

Cartilage is an elastic tissue that compress under mechanical load[32]. This would suggest that an implant of a harder material has to be positioned somewhat recessed in order not to protrude on weight-bearing. In a finite element model developed for sheep the authors[31] actually suggested the ideal position to be some hundred microns below the surface to attain a proper implant level. These authors also pointed to the stabilizing effect on the horizontal compression forces of the surrounding cartilage during cyclic

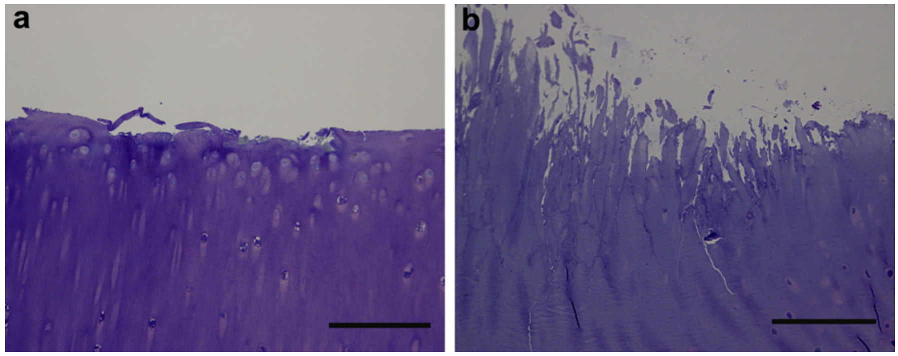

Fig. 6. Histological picture (toluidine blue) of tibial cartilage opposing the implant showing (a) minor cartilage damage (modified Mankin score grade 1), and (b) severe damage (modified Mankin score grade 11). Scale bar = 100 um.

loading. Another factor of equal importance is to accommodate the variation in implant position depending on the surgical imprecision of multi-factorial origin; e.g., surgeon, instrumentation or implant related. Our pilot data, using a first generation of implantation instruments, show that some implants were positioned proud; up to 0.7 mm. Extrapolating from our pilot data we might speculate that two out of the 20 implants would have protruded if all implants were aimed at the 0.3 mm recessed level, and no implants would have protruded if aimed at the maximally recessed 0.7 mm level. We therefore suggest that there is a preferred safe zone of implant position if aimed around 0.5 mm recessed, that could accommodate for all above factors, thus avoiding protruding implants while still offering stability to surrounding cartilage.

A biomechanical study on human cadaveric knees showed markedly elevated tibio-femoral contact pressures when a small metal implant protruded 1 mm compared to flush position or to having no implant[24]. Our finding of severe cartilage damage in the group with protruding implants, expressed as a modified Mankin score of 6–11 (Fig. 7), could be regarded as a morphological confirmation of increased mechanical stress. In a situation with optimized implants and more precise insertion instruments, we foresee that implants could be placed closer to the level of the surrounding cartilage, in agreement with previous biomechanical simulations[31]. This finding further emphasizes the likelihood of mechanical factors as responsible for the cartilage damage. The articulating surface materials where not a purpose of comparison in this study, however, it seemed to be of less importance as no statistical significant difference in Mankin nor ICRS score between the two different biomaterials was found, which in fact is in agreement with previous findings[30].

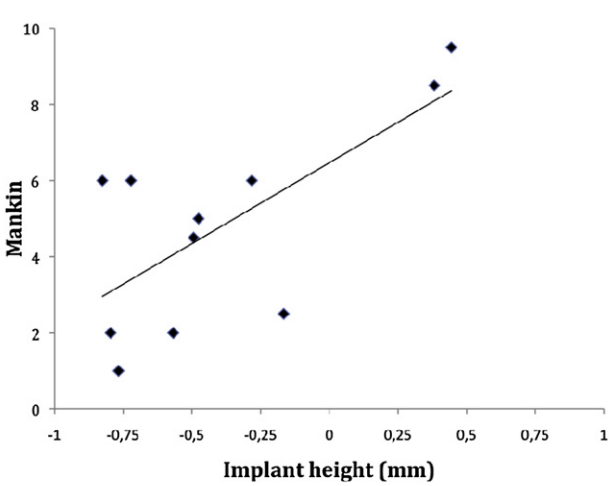

Fig. 7. Implant position in mm relative to the surrounding cartilage level as the independent variable on the *X*-axis and the Mankin score as the dependent variable on the *Y*-axis. Protruding implants show higher Mankin score ($P < 0.01$). Line denotes best fit for least square regression.

Our study was intended as a pilot study and has limitations. We opted for bilateral knee operation for ethical reasons; bilateral operations limit the number of sacrificed animals. Further, double-sided interventions would not compromise the test of this concept, since the animals in this model were prevented from unloading to the contralateral limb, corresponding to a situation with a unilateral intervention. Another limitation is the short follow-up as injuries could develop over time. However, the scope of this pilot study was to relate cartilage damage to implant position and we reasoned that mechanically induced damage would be present at this short term. Furthermore we found no indication of progressive cartilage damage between the 6-week and 3-month controls. We used implants with an articulating surface of either 316L stainless steel or Cr–Co with slightly different configurations. These materials are frequently used in contemporary orthopaedics to articulate against cartilage, i.e., against the patella. Our implants had no sharp edges and hence our interpretation is that the main factor is implant position determining the damage to opposing cartilage. In this first attempt to use laser scanning to assess implant position we used the average height of individual data points for each implant to express the imprecision of surgery and the relation to cartilage damage. Our calculations of the magnitude of implant recess rest on a small number of observations. However, it is reasonable to assume that too much recess is also detrimental, since full thickness cartilage lesions has been shown to be worse than an implant[30]. Further studies should focus on the importance of implant tilt and bonding between implant and surrounding cartilage including long-term results.

Massive research efforts on biological solutions have been made in the last decades using expensive and sophisticated methods while showing inconsistent results[9,10,19,33]. Hence, a number of groups are exploring the FKR concept, where the first study in human knees reports promising results[34]. Our finding of minor damage on the opposing cartilage in the cases where the implant was appropriately inserted confirms that this technology might become of clinical use in the future. We emphasize, however, that metallic implants should never protrude but instead be placed somewhat recessed. Surgical precision by accurate and reliable instrumentation systems is of the utmost importance. Provided this goal is reached, we believe that small metallic implant might give negligible damage to opposing cartilage and we recommend further studies.

Contributions of authors

NM-C: study design, performance of all surgeries, data analyses and writing of the manuscript, HB: data analyses and writing manuscript, KH: histological preparations, HN-S: performance of all surgeries and care of animals, LR: study design, performance of most surgeries, data analyses and writing of the manuscript and A-SL: performance of most surgeries, care of animals, writing part of the manuscript. All authors: review of the manuscript.

Conflicts of interests

One of the authors (LR) serves on the board of the sponsor (Episurf Medical). For this reason he has not participated in the acquisition and handling of raw data. None of the other authors report a conflict of interest.

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